REMARKS

Status of the Prosecution.

Claims 1-35 are currently pending in the application. Claims 14-16 and 18-35 have been withdrawn from consideration as drawn to a nonelected invention, leaving claims 1-13 and 17 presently under consideration. Claims 1, 4-13 and 17 are amended herein and are believed to be in allowable condition. The specification contains support for the amendments made herein, and no new matter has been introduced through the amendments.

Claims 5 and 9 are properly dependent.

Claims 5 and 9 stand objected to as being of improper dependent form for allegedly failing to narrow the scope f the claim from which they depend. The claims as amended clearly narrow the scope of the referenced claim and thus the grounds of the objection are obviated. Applicants respectfully submit that the amended claim satisfies the requirement and thus request that the objection be withdrawn.

The Requirements of 35 U.S.C. § 112, Second Paragraph, Are Met.

Claims 1-13 and 17 were deemed indefinite under 35 U.S.C. § 112, second paragraph in so far as they employ the term "human ß1A

sodium channel subunit" as a limitation. The Office Action alleges that the specification does not identify that property or combination of properties which is unique to, and therefore definitive of "human ß1A sodium channel subunit." Applicants respectfully traverse this requirement.

Applicants have defined, on page 13 of the instant specification, "human ß1A sodium channel subunit" protein as referring to protein which can specifically function as a channel subunit; thus it can combine with other subunits to form a functioning channel. (Applicants' specification at page 13, first full paragraph). The skilled artisan would also understand from Applicants' specification that the protein has a signal sequence, sites for potential N-linked glycosylation, and a transmembrane domain (Applicants' specification, page 53). As shown in Figure 1, The protein is 72% identical to the both the human sodium channel ß1 subunit and the rat VGSC ß1A subunit. In particular, it is 100% identical to the both the rat sodium channel ß1A subunit and the human sodium channel ß1 subunit over amino acids 1-149, but its novel carboxy terminal region from 150-268 is less than 17% identical to the analogous region from human sodium channel ß1 subunit. A human sodium channel ß1A subunit is also 100% identical in its carboxy terminal region (residues 150-268) to the

human EST database Accession Number AI742310. Contrary to assertions in the Office Action, Applicants submit that this identifying information informs one of skill in the art exactly what a human sodium channel ß1A subunit is, and clearly differentiates it from the related protein, human sodium channel ß1 subunit. The skilled artisan can readily and clearly determine if a given compound is included or excluded from the claimed subject matter. This is even more clear for the claims as amended. Thus, Applicants request withdrawal of this rejection to the claims under 35 U.S.C. § 112, second paragraph.

Claims 5, 7, and 9-13 were deemed indefinite because the metes and bounds of the terms allelic variants, mutants and functional derivatives were considered undeterminable. The Office Action alleges that, for example, "allelic variants" can include the complete absence of a gene product. It also alleges that it is unclear how a functional derivative differs from the human sodium channel ß1A subunit. Applicants respectfully traverse this rejection.

Applicants have amended the claims to remove the term "mutants" for clarification. The specification clearly defines allelic variants and functional derivatives on pages 23 and 24 (see also discussion regarding enablement). Applicants

respectfully submit that reading the claims in view of the teachings, one of skill clearly understand the metes and bounds of the claims. The terms allelic variants are expressly defined in the specification on pages 23-24. While the assertion in the Office Action regarding complete absence of the gene product may true in a general sense in the art, here, one of skill in the art could not read Applicants' claims in view of the definitions in the specification to include the possibility of no gene product, as the interpretation would render the claim meaningless. Similarly, the term "functional derivative" is clearly defined in the specification on page 24. Applicants are entitled to be their own lexicographers. Skilled artisans would understand that in order to possess a structural or functional activity of a human sodium channel ß1A subunit, any differences between the claimed compounds and the given sequence would have to limited, particularly where the closer an encoding polynucleotide sequence is to SEQ ID NO:14, the more highly preferred the compound. Applicants therefore submit that the metes and bounds of the terms, and particularly of the claims containing them, are clearly defined. Applicants thus respectfully request reconsideration of the rejection under 35 U.S.C. § 112, second paragraph and withdrawal of the same.

Claims 4, 5, 8, and 12 were deemed confusing because it was allegedly unclear if the sequence identifiers contained within the parentheses were exemplary or limiting. The claims have been amended to clarify any typographical or other errors that resulted in the presence of the parentheses, thus rendering moot the grounds of the rejection. Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 112, second paragraph with respect to these claims.

Claim 6 was deemed vague and indefinite for the recitation of "said DNA" with no antecedent basis. Claim 6 as amended is believed to contain proper antecedent basis for all claims elements or limitations. The rejection therefore should be overcome. Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 112, second paragraph with respect to this claim as well.

Claim 17 was deemed vague and indefinite for the recitation of the allegedly conditional limitation "stringent hybridization conditions." The claim has been amended to specify the hybridization conditions as exemplified on page 26 of the specification. Since the grounds of the rejection have been obviated, Applicants request withdrawal of the rejection under 35 U.S.C. § 112, second paragraph with respect to this claim.

The Specification Enables the Skilled Artisan to Make and Use the Claimed Invention.

Claims 1-3, 5-7, 9-13 and 17 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly containing subject matter which was not described in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants respectfully traverse the rejection.

The claims are generally directed to an isolated polynucleotide encoding a human ß1A sodium channel subunit protein, wherein the polynucleotide is selected from the group consisting of: (a) a polynucleotide encoding SEQ ID NO:14, (b) a polynucleotide comprising amino acids 150 to 268 of SEQ ID NO:14, and (c) a polynucleotide which is complementary to the polynucleotide of (a) or (b).

Claims are further directed to polynucleotides of RNA, DNA, and genomic DNA; polynucleotides of SEQ ID NO:12 or SEQ ID NO:13, and allelic variants thereof encoding SEQ ID NO:14. Claims are also directed to expression vectors and host cells containing the claimed polynucleotides, as well as a process for expressing human

ß1A sodium channel subunit protein in a host cell using the polynucleotides.

The question of enablement is a question of law, based on underlying factual determination. *Amgen, Inc. v. Hoechst Marion Roussel, Inc. et al.*, 314 F.3d 1313,1334 (Fed. Cir. 2003). Before any analysis of enablement can occur, it is necessary for the examiner to construe the claims. The examiner should always look for enabled, allowable subject matter and communicate to Applicants what that subject matter is at the earliest point possible in the prosecution of the application. (MPEP 2164.04) The Federal Circuit has consistently held that "the specification must teach those of ordinary skill in the art how to make and use the full scope of the invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1561 (Fed. Cir. 1993). The specification need not explicitly teach those in the art to make and use the invention; the requirement is satisfied if, given the what they already know, the specification teaches those skilled in the art enough that they can make and use the invention without "undue experimentation." *Amgen*, 314 F.3d at 1334. The fact that a quantity of experimentation, even complex experimentation, may be required is not dispositive of the analysis (MPEP 2164.04). The key word is "undue," not "experimentation". *In re Angstadt*, 537

F.2d 498,504 (CCPA 1976). The factors to be considered in determining whether experimentation is undue include the breadth of the claims; the nature of the invention; the state of the prior art; the level of one of ordinary skill; the level of predictability in the art; the amount of direction provided by the inventor; the existence of working examples; and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). It is improper to conclude that a disclosure is not enabling based on analysis of only one of the factors while ignoring one or more of the others. MPEP 2164.01(a). Nevertheless, not everything necessary to practice the invention need be disclosed. The Federal Circuit has stated that what is well-known is best omitted. *In re Buchner*, 929 F.2d 660, 661 (Fed. Cir. 1991). Further, the scope of enablement must only bear a reasonable connection to the scope of the claims. *See, e.g., In re Fisher*, 427 F.2d 833, 839 (CCPA 1970). Additionally, as the Federal Circuit recently reiterated, the law is clear that the specification need teach only one mode of making and using a claimed composition. *Amgen*, 314 F.3d at 1335.

Applicants respectfully submit that the skilled artisan, having only the sequences and teachings of the instant

specification is readily enabled to make and use the claimed invention.

As the claims stand, they are drawn to a very small group of defined nucleotides which encode functional proteins heretofore unknown. Notwithstanding allegations to the contrary, Applicants' specification, as discussed above, defines "human ß1A sodium channel subunit" protein as referring to protein which can specifically function as a channel subunit; thus it can combine with other subunits to form a functioning channel. (Applicants' specification at page 13, first full paragraph). Additionally, variants of polynucleotides are described as differing from a reference polynucleotide, but generally containing differences limited so that the nucleotide sequences of the reference and the variant are closely similar overall and in many regions identical. Applicants' Specification, page 23-24. Given that the Office Action acknowledges that no prior art disclosing or suggesting the claimed sequences has been identified, Applicants' specification is entitled to dominate future patentable inventions based in some was on their teachings, since the improvements, while unobvious were made possible by their work. *In re Fisher*, 427 F.2d 833 (CCPA 1970). Given the narrow scope of the claims, Applicants' specification provides more than a reasonable correlation to the

scope of enablement provided and further given the high level of skill in the art, Applicants respectfully submit that the claims are fully enabled.

The Office Action alleges that the instant specification does not identify those amino acid residues in SEQ ID NO:14 which are critical to the structural and functional integrity of a human ß1A sodium channel subunit protein, nor identify any structurally analogous protein. The Office Action also provides some calculations regarding the alteration of nucleotide and amino acid sequences, including the allegation that claim 1 encompasses a human ß1A sodium channel subunit protein whose amino acid sequence can deviate from SEQ ID NO:14 by as many as 201 out of the 268 amino acids residues. This is contrary to Applicants' definition of human ß1A sodium channel subunit protein and completely inconsistent with the claims read in view of the specification. Additionally, while these calculations are unsupported by any reference, they appear to be intended to suggest that even minimal changes in a nucleotide sequence drastically alter the structure and function of an encoded protein. This is simply contrary to the teachings of the art. Applicants submit herewith a copy of a paper by Service (Science, 277: 179, 1997) which teaches that if a new gene's protein product resembles a known one at 30% of its

amino acid positions or more, it is considered very likely to have a similar shape and function. Given the guidance in the specification as to the function (e.g. page 23-24) (as well as ways to measure the function (see e.g. pages 31-37)), and detailed description of structure of the subunit (primary and secondary structure (see e.g. Example 2), and comparisons to other known sequences (e.g. pages 53-54), one of skill in the art could readily identify locations not likely to be critical residues and modify them to generate "functional derivatives" (defined in the specification on page 24 as "a compound that possesses a biological activity (either functional or structural) that is substantially similar to the biological activity of human ß1A sodium channel subunit.").

Additionally, Applicants have added structural limitations, specific hybridization conditions and other clarifying language to the claims, for example to claims 7, 10 and 11.

Thus, given the scope of the amended claims, the corresponding scope of enablement of the specification, and the high level of skill in the art, Applicants respectfully submit that the claims are more than fully enabled. Proper reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph is respectfully requested.

The Claimed Invention is Adequately Described in the Specification.

Claims 1-3, 5-7, 9-13 and 17 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly not described in the specification in such a way as to reasonably convey to a skilled artisan that the inventors were in possession of the claimed invention at the time of filing. Applicants respectfully traverse this rejection.

The Office Action alleges that the claims are directed to a very large genus of polynucleotides encoding any protein which is encompassed by the term human ß1A sodium channel subunit. The Office Action further alleges that under the holding in *Eli Lilly*, a precise definition of the structure is required. However, the Federal Circuit has clarified the legal standard set forth in *Eli Lilly*.

The adequacy of a written description is a question of fact which must be determined on a case-by case basis. MPEP 2163. A written description is given a strong presumption of adequacy and rejection of original claims for lack of written description should be rare. *Id.* An examiner must overcome the presumption of adequacy by putting forth, on a reasonable basis, sufficient

evidence or reasoning. *In re Wertheim*, 541 F.2d 257, 263 (CCPA 1976). Arguing lack of literal support is not enough since the invention need not be described *in ipsis verbis* to satisfy the written description requirement. *Id.* at 265.

As the Federal Circuit has stated: ". . .the applicant must also convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." *Vas-Cath Inc. et al. v. Mahurkar et al.*, 935 F.2d 1555, 1563-4 (Fed. Cir. 1991) (emphasis in original). See also *Regents of the Univ. of Cal. v. Eli Lilly & Co.*, 119 F.3d 1559, 1566 (Fed. Cir. 1997). A preponderance of evidence is required as to why a skilled artisan would not recognize a description of the claimed invention, as that is the perspective from which satisfaction of the requirement is measured. *Amgen Inc. v. Hoechst Marion Roussel, Inc. et al.*, 314 F.3d 1313, 1330 (Fed. Cir. 2003) (citing *Lockwood v. Am. Airlines, Inc.*, 107 F.3d 1565, 1572 (Fed. Cir. 1997)); see also MPEP 2163. The written description inquiry, therefore, focuses on a comparison between the specification and the invention referenced by the terms of the claim. *Id.* at 1332.

Possession of the invention may be established through words, structures, figures, diagrams and formulas which fully set forth the claimed invention. *Lockwood*, 107 F.3d at 1572. "Generally there is an inverse correlation between the level of skill and knowledge in the art and the specificity of the disclosure necessary to satisfy the written description requirement." MPEP 2163.

Furthermore, the Federal Circuit has steadfastly refused to require sequences in all cases of claims to genetic material. "[M]ore recently in *Enzo Biochem*, we clarified that *Eli Lilly* did not hold that all functional descriptions of genetic material fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure." *Amgen*, 314 F.3d at 1332.

In the instant application, the structure of the encoded polypeptides is compared and contrasted with the well-characterized human sodium channel ß1 subunit and other proteins, in combination with the well-described or exemplified steps of cloning, characterizing and assaying the encoded polypeptides provides information more than sufficient to convince a skilled artisan that Applicants were in possession of the claimed

invention. In particular, one of skill in the art would recognize that Applicants were in possession of the common attributes or features of the elements possessed by members of the genus based on the information disclosed and the methods for generating additional genus members from the additional sequences provided. More importantly, the high degree of identity between the amino terminal portion of the human sodium channel ß1A subunit and the human sodium channel ß1 subunit, versus the very low homology at the carboxy terminal portion of the molecule provides a powerful description of the genus of polynucleotide molecules claimed (see *supra*, discussion on enablement). The skilled artisan can readily envision the structure of molecules of the claimed genus. In accordance with the holding in *Amgen*, sufficient information has been conveyed such that those of skill in the art would recognize the description of the molecules. The specification conveys to those of skill in the art distinguishing information concerning the identity of the molecules such that one of skill could visualize or recognize the identity of the members of the genus of claimed nucleic acids. For example, the specification discloses the functional information, as well the structural information required for the skilled artisan to correlate the function with known structures - i.e. descriptions of both the sodium channel

function and ability to associate with other proteins to form the channel as well the primary and secondary structural information. Nothing more is required under 35 U.S.C. § 112, first paragraph or under the Guidelines for Written Description.

The Office Action must properly weigh all factors including partial structure, physical/chemical properties, functional characteristics, known or disclosed correlations between structure and functions, methods of making, and combinations of the above in view of the level of skill and knowledge in the art in determining whether one of skill would recognize that applicant was in possession of the invention. The specification describes the polynucleotides sufficiently so as to satisfy the written description requirements 35 U.S.C. §112, as well as the policies behind it. The specification clearly conveys that the Applicants have invented the claimed subject matter; the public is put in possession of what was invented; and there is a *quid pro quo* for the patent rights sought. In view of the foregoing, the Applicants respectfully request the withdrawal of the rejection for lack of adequate written description under 35 U.S.C. §112.

Claims 5, 6, 8 and 10 stand rejected under 35 U.S.C. § 112, first paragraph for allegedly failing to describe a genomic DNA encoding "human ß1A sodium channel subunit" or a polynucleotide

encoding the same. Applicants respectfully traverse this requirement. The Office Action also alleges that there is absolutely no description of an isolated polynucleotide which encodes a human ß1A sodium channel subunit in the antisense direction. Applicants have amended the claims to clarify that the claims do not require a polynucleotide which encodes a human ß1A sodium channel subunit in the antisense direction.

Applicants respectfully submit that a genomic DNA encoding a human ß1A sodium channel subunit is adequately described in the instant specification, for example, see the Brief Description of Drawings on page 8 (description of figure 2), as well as Figure 2 and the information in Example 1, for example at page 54, wherein a description of genomic DNA for both human ß1 sodium channel subunit, as well as human ß1A sodium channel subunit are found. In view of the amendments and the foregoing, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph with respect to these claims.

Claim 17 also stands rejected under 35 U.S.C. § 112, first paragraph for allegedly failing to require the presence of any nucleic acid encoding a human ß1A sodium channel subunit. The claim has been amended to clarify that the expression vector

encodes a human ß1A sodium channel subunit. Accordingly, Applicants respectfully request withdrawal of the rejection with respect to this claim.

Conclusion.

Applicants believe the present paper to be fully responsive to all outstanding issues. The current amendments are considered to place all the claims in condition for allowance and the same is earnestly sought in an early and favorable action. Should the examiner have any questions, he is invited to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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